Analysis of clinical characteristics in large-scale Chinese women with polycystic ovary syndrome

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Summary

OBJECTIVE: To analyze the clinical and metabolic characteristics of large-scale Chinese women with polycystic ovary syndrome (PCOS). **DESIGN:** Retrospective study. **SETTING:** Hospital-based IVF center. **PATIENT(S):** Patients with PCOS. **METHODS:** In the present study, one thousand and forty PCOS patients were selected from women who visited the Reproductive Medicine Center at Shandong Provincial Hospital Shandong University between January 2002 and December 2006. All the patients had been performed a 75g OGTT. Clinical characteristics, serum hormonal levels, glucose levels, insulin levels and lipid profiles were reviewed. **INTERVENTIONS:** An oral glucose tolerance test and insulin release test were performed for each woman. After overnight fasting, blood samples were collected to determine fasting blood glucose, blood glucose and insulin (30min, 60min, 120min, 180min) after digesting 75g glucose, luteotrophic hormone (LH), follicle-stimulating hormone (FSH), testosterone (T), prolactin (PRL), estradiol (E_2), and blood lipid levels. **MAIN OUTCOME MEASURES:** Height, weight, waistline, hip circumference, F-G grade for hirsutism, gonadal hormone results, blood lipid level, blood glucose tolerance, each-moment insulin level, and family history were determined. **RESULTS:** (i) The presence of oligomenorrhea was 62.6% while amenorrhea was 19.71%. Menstrual disorder of all the adult patients could be traced back to their adolescent menarche. There were 450 obesity cases of which 259 patients were central obesity. The incidence of acanthosis nigricans was 15.19%, 65.19% with obesity. (ii) Cholesterol (4.8 ± 0.98 vs 4.61 ± 0.86) and LDL (3.80 ± 6.92 vs 2.88 ± 1.01) were both significantly higher in the obesity patients than the non obesity patients. (iii) 173 patients were diagnosed as diabetes mellitus (DM), 179 IGT, 27 IFG and 9 (IFG and IGT). Those women with plasma glucose values abnormality of 0, 30min, 60min, 120min, 180min were 19 cases 0.98% (19/173), 74 cases 42.77% (74/173), 110 cases 63.58% (110/173), 42 cases 24.28% (42/173) and 12 cases 6.94% (12/173) respectively. Ten (10/173) patients would have been undetected if fasting plasma glucose levels were not evaluated, while omission of 30min, 60min, 120min, or 180min plasma glucose levels would have resulted in 16 cases (16/173), 50 cases (50/173), 28 cases (28/173) and 1 case (1/173) being missed respectively. If we took three times blood samples

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to evaluate plasma glucose levels, 39 cases (39/173) (0min + 30min +60min), 102 cases (0min + 30min + 120min), 21 cases (0min + 30min + 180min), 34 cases (0min + 60min + 120min), 45 cases (0min + 60min + 180min), 123 cases (0min + 120min + 180min) would be missed. Compared AUC of plasma glucose and insulin in 5 times with 3 times (0min + 30min + 60min), the differences were statistically significant. Body mass index (BMI) was positively correlated with HOMA-IR (r = 0.29987 (P<0.01) as well as WHR (r = 0.12441, P<0.0001).

CONCLUSIONS: (i) The prevalence rate of obesity was higher in PCOS. The state of obesity had a positive relation with insulin resistance. (ii) The prevalence rate of lipid profiles abnormality in obesity group was higher than in non-obesity. (iii) OGTT was the essential examination for all the PCOS patients.

Abbreviations (Alphabetical order):

AUC – area under curvel
BMI – body mass index
E_2 – estradiol
FINS – fasting insulin
FPG – fasting plasma glucose
FSH – follicle-stimulating hormone
HDL – high density lipoprotein
HOMA – Homeostasis Model Assessment
HOMA- IS – Homeostasis Model Assessment-insulin sensitiveness
HOMA- IR – Homeostasis Model Assessment insulin resistance
IFG – impaired fasting glucose
IGT – Impaired glucose tolerance
IR – insulin resistance
LDL – low-density lipoprotein
LH – luteotrophic hormone
NIDDM – non- insulin-dependent diabetes mellitus
OGTT – oral glucose tolerance test
PCOS – Polycystic ovary syndrome
PRL – prolactin
SPSS – the Statistical Package for the Social Sciences
T – testosterone
WHO – world health organization
WHR – waist hip ratio
WL – waistline

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in reproductive-aged women, affecting at least 1 in 15 women during their reproductive life [1]. Currently, the most commonly used definition of PCOS includes at least two of the three following criteria: clinical and/or biochemical signs of hyperandrogenism, olig-ovulation and/or an-ovulation, and polycystic ovary under ultrasonography (excluding other related diseases, such as adrenal congenital hyperplasia, Cushing's syndrome, androgen-secreted tumors) [2, 3]. The pathology of PCOS is heterogeneous, and it is extremely difficult to elucidate the precise mechanisms of the disease. But it was confirmed that insulin resistance is present in PCOS patients [4, 5]. Insulin resistance is now recognized as a major risk factor for the development of type 2 (non-insulin-dependent) diabetes mellitus (NIDDM) [6]. PCOS women would thus be predicted to be at an increased risk for NIDDM [12]. Impaired glucose tolerance (IGT), a state characterized by mild elevations in blood glucose levels, typically antedates the onset of NIDDM.

Most of the data about insulin resistance in PCOS women were available from small-scale studies. There were no reports about large-scale analysis of the prevalence and characteristics of insulin resistance in Chinese PCOS patients. And there was no similar analysis about whether the OGTT is essential to the PCOS patients. So we studied the clinical characteristics of the metabolism in 1040 Chinese PCOS patients in order to provide powerful evidence.

MATERIALS AND METHODS

Clinical detection

This retrospective study included 1040 PCOS patients who visited the Reproductive Medical Center at Shandong Provincial Hospital, Shandong University, between January 2002 and December 2006. All patients enrolled in this study were diagnosed according to the Rotterdam consensus workshop criteria of 2003 [1, 2]. A standardized history form was completed, with emphasis on menstrual dating and regularity, hirsutism and acne, gynaecological history, medications and family history.

This study was based on routine clinical practice. The protocol of this study was approved by the Ethics Committee of Shandong University, and informed consent was obtained from individuals who participated in this study.

Clinical features were recorded and included anthropometric variables such as body height, weight, waistline, hip circumference, the degree of hirsutism (Ferriman-Gallwey scale), family history (diabetes mellitus or hypertension in first-degree relative), menstrual cycle, and endocrine biochemical parameters. Trans-vaginal ultrasound (LogIQ-200 Pro series ultrasonic machine, GE Company, USA) was used to detect polycystic ovaries, defined as the presence of at least one ovary >10 ml or at least 12 follicles 2–9 mm in diameter. Ultrasound examination was performed through the anus when subjects were unmarried (virgin) girls.

BMI was calculated using the formula [weight (kg)/height^2 (m^2)] (Cooperative Meta-Analysis Group of China Obesity Task Force, 2002). The criteria of the International Life Science Association of China were applied: (i) BMI <25: normal; (ii) BMI ≥25: obesity.

Serum sex hormone analysis

All patients were subjected to fasting blood serum sex hormone examinations. Serum hormone levels were obtained during Day 2–6 of their menstrual cycles (natural or bleeding after progestin withdrawal). If the patient had amenorrhea, the examination was performed after confirming there was no dominant follicle by ultrasound. Serum sex hormones, including follicle-stimulating hormone (FSH), luteotrophic hormone (LH), prolactin

(PRL), testosterone (T), and estradiol (E_2), were detected by chemiluminescence immunization (Beckman Access Health company, USA).

Metabolic examinations

All subjects underwent an oral glucose tolerance test (75 g), insulin-releasing curve, and blood-lipid examination. First, fasting blood was obtained for glucose and insulin measurements. After taking glucose, blood was tested at 30 min, 60 min, 120 min, and 180 min. Glucose tolerance was detected by the glucose oxidase method (AU640 automatic biochemistry analyzer and their relevant reagent, Olympus Company, German), and the insulin-releasing curve was detected by chemiluminescence. We also determined levels of serum total cholesterol, triglycerides, and low-density lipoprotein (LDL) to reflect blood-lipid level.

According to the WHO criteria for IGT and NIDDM, determinations of glucose tolerance were made as follows: normal fasting glucose = FPG <100 mg/dl (5.6 mmol/l), impaired fasting glucose = FPG ≥100 mg/dl (5.6 mmol/l) but ≤125 mg/dl (6.9 mmol/l), provisional diagnosis of diabetes = FPG ≥126 mg/dl (7.0 mmol/l), NGT = 2-h post-oral glucose load (2-h PG) <140 mg/dl (7.8 mmol/l), IGT = 2-h PG ≥140 mg/dl (7.8 mmol/l) but <200 mg/dl (11.1 mmol/l) and provisional diagnosis of diabetes = 2-h PG ≥200 mg/dl (11.1 mmol/l) [7, 8].

Index evaluating and methods

HOMA was calculated according to the formula [plasma glucose (mmol/l) × insulin (μU/ml)]/22.5 [9]. AUC (5) = 0.25*glucose (0min) + 0.5* glucose (30min) + 0.75*glucose (60min) + glucose (120min) + 0.5*glucose (180min), AUC (3) = 0.25* glucose (0min) + 0.75*glucose (60min) + 0.5*glucose (120min).

Evaluate the function of insulin β-cell with HOMA-IS: HOMA-IS = 20*FINS/ (FPG–3.5). $^{\Delta}$I30/$^{\Delta}$G30: The ratio between insulin (30min) minus insulin (0min) and glucose (30min) minus glucose (0min).

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows version 11.0 (SPSS Inc., Chicago, IL, USA), and statistical significance was considered at the two-tailed 0.05 *P* level. Homogeneity tests for variance, independent sample *t*-test, and contingency table χ^2 criterion were performed when necessary.

RESULTS

A total of 1040 PCOS were studied in our research. The subjects were from the same ethnic backgrounds, and average age 28.29 years, ranged from 16 to 42 years. BMI was 24.77 ± 4.71 (kg/m^2), WL 82.85 ± 10.86 cm, Hip circumference 97.16 ± 9.5 cm, WHR 0.85 ± 0.06. See table 1.

Patients were classified by BMI as following: there were 450 PCOS patients, whose BMI ≥25kg/m^2 (obesity) and 590 PCOS women whose BMI <25kg/m^2 (non obesity). There were 450 obesity cases, of which 259 abdominal obesity. The incidence of acanthosis nigricans was 15.19% (158/1040), of which 65.19% (103/158) with obesity and 34.81% (55/158) with non-obesity.

The prevalence of oligomenorrhea was 62.60% (651/1040), amenorrhea was 19.71% (205/1040) and normal menstrual cycle was 13.85% (144/1040). Menstrual disorder of all the patients could be traced back to their adolescent menarches. The prevalence of hypertriglyceridemia was 5.58% (58/1040) while hypercholesteremia was 7.02% (73/1040, abnormality of HDL was 0.10% (1/1040) and abnormality of LDL was 12.69% (132/1040). Cholesterol (4.8 ± 0.98 vs 4.61 ± 0.86) and LDL (3.80 ± 6.92 vs 2.88 ± 1.01) were both significantly higher in the obesity patients than in the non obesity patients. HOMA-IS was of no statistical difference between the obesity and non obesity patients.

173 patients were diagnosed as diabetes mellitus (DM) according to National Diabetes Data Group (NDDG) criteria, 179 IGT, 27 IFG and 9 (IFG and IGT). Those women with plasma glucose values abnormality of 0, 30min, 60min, 120min, 180min were 19 cases 0.98% (19/173), 74 cases 42.77% (74/173), 110 cases 63.58% (110/173), 42 cases 24.28% (42/173) and 12 cases 6.94% (12/173) respectively. Ten (10/173) patients would have been undetected if fasting plasma glucose levels were not evaluated, while omission of 30min, 60min, 120min, or 180min plasma glucose level would have resulted in 16 cases (16/173), 50 cases (50/173), 28 cases (28/173) and 1 case (1/173) missed diagnoses respectively. If we took three times blood samples to evaluate plasma glucose

Table 1. The base resource of patients with PCOS

	mean	SD
Age (year)	28.29	3.49
BMI (kg/m2)	24.77	4.71
W/H	0.85	0.06
LH/FSH	1.55	0.97
Glucose (0) (mmol/l)	4.92	1.03
Glucose (30`) (mmol/l)	8.54	2.07
Glucose (60`) (mmol/l)	8.54	2.84
Glucose (120`) (mmol/l)	7.01	2.24
Glucose (180`) (mmol/l)	5.21	2.17
Insulin (0`) (mIU/ml)	9.92	7.83
Insulin (30`) (mIU/ml)	71.38	48.18
Insulin (60`) (mIU/ml)	82.76	60.22
Insulin (120`) (mIU/ml)	67.31	55.56
CHO (mmol/l)	4.67	0.92
TG (mmol/l)	1.04	0.77
HDL (mmol/l)	1.73	0.64
LDL (mmol/l)	2.96	1.10

levels, there would be 39 cases (39/173) (0min + 30min + 60min), 102 cases (0min + 30min + 120min), 21 cases (0min + 30min + 180min), 34 cases (0min + 60min + 120min), 45 cases (0min + 60min + 180min), 123 cases (0min + 120min + 180min) missed.

We compared AUC of plasma glucose and insulin in 5 times with that in 3 times (0min + 30min + 60min), and found the differences were statistically significant. Body mass index (BMI) was positively correlated with HOMA-IR (r = 0.29987, $P<0.01$) as well as WHR (r = 0.12441, $P<0.0001$).

DISCUSSION

In this study, we can note that PCOS was always accompanied with IR, and the prevalence of IR with obesity was much higher than that without obesity. Also, we found that FINS and HOMA-IR were higher in obesity PCOS patients than in non-obesity, which exhibited the extent of IR with obesity was more severe than with non-obesity. Furthermore, the former levels of triglyceride were higher than the latter which means the lipid metabolism disorders were more severe. We evaluated the function of β-cell with HOMA-IS and found there was no statistical difference between two groups. This indicated the secretion ability of β-cell had a strong reservation during this age range and it remained compensative.

Our data indicated that the prevalence rate of impaired glucose tolerance in Chinese PCOS (IGT 17.21%)) was lower than that of American PCOS women (IGT 31%), but the prevalence rate of NIDDM in Chinese PCOS (16.63%) was higher than that of American PCOS women (7.5%) (10). the prevalence rate of IGT and NIDDM in PCOS patients was significantly higher than that of the general population (11). Although some differences among these studies in the selection criteria of PCOS cannot be ignored, the factors of ethnic background, dietary composition and lifestyle may play an important role in the prevalence of abnormal glucose tolerance in PCOS.

We found that ten NIDDM patients would have been undetected if fasting plasma glucose levels were not evaluated, while omission of 30min, 60min, 120min, or 180min plasma glucose level would have resulted in 16 cases, 50 cases, 28 cases and 1case being missed respectively. If we took three times blood samples to evaluate plasma glucose level, 39 cases (0min + 30min + 60min), 102 cases (0min + 30min + 120min), 21 cases (0min + 30min + 180min), 34 cases (0min + 60min + 120min), 45 cases (0min + 60min + 180min), 123 cases (0min + 120min + 180min) would have been missed without performing an OGTT. Though OGTT is time-consuming and inconvenient, we recommend all the PCOS patients conduct OGTT. Accordingly, PCOS is regarded as a risk factor for the development of T2DM and general screening of PCOS patients for IGT and/or T2DM has been recommended. Thus, an OGTT appears to be the only way to reliably detect abnormal glucose metabolism in PCOS.

In summary, disorders of metabolism in obesity PCOS patients were more serious than in non-obesity. Obesity amplifies the extent of IR. OGTT is the essential examination for all the PCOS patients.

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